



## Pharmacological Treatment of Acute Dental Pain

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### INTRODUCTION

Prevention and management of dental pain is an integral part of endodontic treatment. Meta-analysis and clinical trials indicate that postoperative pain can occur in 8–40% of all endodontic patients (1, 2). Postoperative pain has been associated with intensity of preoperative pain and is most likely to occur within the first 24 hours after treatment (3). In order to minimize and manage postoperative acute dental pain, the clinician should consider the administration of analgesics. Recent changes for dosing of analgesics can lead to confusion between patients and providers. This clinical update presents information for the use of analgesic medication in managing acute postoperative dental pain including updated maximum dosage information for common analgesics.

### CLINICAL USE OF ANALGESICS

It is important to assess pain from several perspectives before deciding on the appropriate analgesic. The following criteria are suggested: (a) the extent of the surgical procedure; (b) the psychological make-up of the patient; (c) the patient's past experience with analgesics; and (d) the planned activity of the patient in the next 24 to 48 hours. When dental pain is mild to moderate, most patients can be managed and do well with peripherally acting analgesics (non-narcotic). These analgesics suppress pain perception by blocking or reducing noxious input into the central nervous system (CNS) (4). A centrally acting analgesic (opioid/narcotic) should be considered when pain becomes more intense or if their quality of life is altered such that a mood-altering medication is required. Analgesics include non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen (Tylenol™), opioid agonists and combination medications of peripherally acting with centrally acting medications (4).

### NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

NSAIDs are frequently the first analgesic used for the management of dental pain. The use of NSAIDs in managing mild to moderate dental pain has been shown to be effective (5). However, despite increasing the dose of the medication, the patient may not experience sufficient relief. This is referred to as the plateau or 'ceiling effect' (6,7). Supplementing the initial dosage with another medication, that acts in an alternative manner, may allow sufficient analgesia to be achieved. Therefore, an NSAID alone may have limited activity against moderate to severe pain (7). Other limitations include potential adverse effects of NSAIDs, including peptic ulcer disease, gastrointestinal (GI) bleeding, GI perforation, impaired renal function and inhibition of platelet function. NSAIDs are also contraindicated in asthmatics as 10–20% have a sensitivity that can precipitate an asthma attack. (7).

**Ibuprofen** is a nonselective cyclooxygenase (COX) inhibitor that inhibits both COX-1 and COX-2 enzymes. This inhibition impairs the transformation of arachidonic acid to prostaglandins, prostacyclin and thromboxanes which cause pain, inflammation and fever.

Ibuprofen produces a dose-related analgesia over the range of 200–800mg. Thus, increasing the dose will produce an increasing magnitude of analgesia (8). Although the 800mg dose pro-

duces maximum analgesic effects, clinicians should only consider this dose if the benefit for treating severe intense pain outweighs the increased risks of adverse effects. Under most conditions, 400–600mg of ibuprofen taken every six hours is sufficient for treating moderate inflammatory pain (8). Ibuprofen is readily absorbed after oral administration and peak blood levels occur about one to two hours after ingestion. Adverse effects of ibuprofen include GI complaints and somnolence. The over the counter (OTC) maximum dose is 400 mg/dose up to 1200 mg per day. Under medical direction, the maximum dose for adults is 800 mg/dose with maximum daily dose of 3200 mg based on an individual's response and tolerance (7).

**COX-2 inhibitors**, derived from NSAIDs, work by targeting the reduction of chemicals that promote inflammation, pain and fever known as prostaglandins (9). COX-2 inhibitors are therefore as effective as other NSAIDs when treating inflammation, pain and fever while reducing adverse effects such as ulcers and decreasing the risk of bleeding. However, in the management of acute dental pain, COX-2 inhibitors are no more effective in relieving surgically induced dental pain, are more expensive and contribute to increased cardiovascular and cerebrovascular morbidity and mortality in susceptible patients (9). Therefore, COX-2 inhibitors are not recommended as an analgesic for acute dental pain.

**ACETAMINOPHEN (APAP)** is widely used as an analgesic and antipyretic and is commonly used to control odontogenic pain but has weak anti-inflammatory activity (6). Acting through a different mechanism than other analgesics, APAP is effective in combination therapy with other NSAIDs or narcotics and is taken by more than 50 million Americans weekly. APAP has few side-effects or contraindications and can be used in patients who cannot take NSAIDs (10). In 2009, the Food and Drug Administration (FDA) reviewed the relationship of APAP use to liver toxicity. Liver toxicity related to APAP overdose had increased by more than 20%. The FDA review brought about changes to the dosing and labeling of prescription medications containing APAP beginning in 2011 (10).

Patients can accidentally exceed the recommended dose by taking multiple medications simultaneously. OTC labels may not spell out the entire acetaminophen and may use an abbreviation such as APAP. Safety information from the FDA on the use of APAP can be found at: <http://www.fda.gov/>. To reduce accidental overdose and hepatotoxicity, the manufacturer, McNeil consumer healthcare division, has voluntarily reduced the maximum daily dose for OTC acetaminophen to 3,000 mg per day. The FDA has recommended a reduction in the maximum single dose to 650mg with a 6 hour interval between doses. With medical direction, 325–650 mg/dose can be administered with a maximum daily dose of 4,000mg.

**OPIOIDS** can relieve practically all forms of pain, including visceral and severe pain. At therapeutic doses, opioids are associated with side effects such as vomiting, sedation, sleep disturbances, drowsiness, dizziness, euphoria, lightheadedness and nausea. At higher dosages, respiratory depression is a risk while chronic administration may cause urinary retention and constipation. Prolonged administration, greater than two to three weeks, promotes tolerance and dependency. This situation should not occur in treating acute dental pain as

administration should not last beyond definitive care. Treatment beyond a reasonable amount of time may indicate a chronic pain condition and require a referral. The "first pass effect", after oral administration, converts 50 - 95% of opiate/opioid drugs to inactive metabolites in the liver. Since the liver metabolizes the drug first, most of the orally administered dose never reaches the brain in an active form. Patients have different first pass efficiencies and brain receptor sensitivities; therefore, the clinical effects of these drugs by the oral route can be unpredictable. The benefit of opioid analgesics is the lack of a plateau effect like NSAIDs, meaning that increased dosing provides more pain relief; however the benefit must be weighed against the risk of respiratory depression (11).

COMBINATION THERAPY

Drug combinations have synergistic effects by targeting different pharmacological pathways. Combining medications can have additive analgesic effects as well as decreased side effects. Combination drug therapy has been used for clinical management of acute pain and studies confirm their effectiveness in post-operative endodontic pain (5). The combination of ibuprofen and acetaminophen has been shown to be more effective at reducing postoperative pain than ibuprofen alone in patients with mild to moderate acute dental pain (5, 12-13). The combination of acetaminophen with an NSAID provided superior and prolonged analgesia with fewer side effects when compared with the combination of acetaminophen and codeine (12). In an *in-vivo* endodontic model, the combination of acetaminophen 1000 mg and 600mg of ibuprofen also demonstrated superior pain control in mild to moderate pain when compared with that achieved when either drug was used separately. In comparison, ibuprofen and the ibuprofen/APAP group reported mean pain intensity reductions of 76% and 96%, respectively (5). For patients who presented with moderate to severe preoperative pain, the use of the NSAID/APAP combination showed no significant difference to those with an ibuprofen regimen alone. In severe pain, the addition of an opioid may be needed (13). The addition of a centrally acting medication may break the plateau effect reached with peripheral analgesics in patients with moderate to severe pain. The opioid/NSAID combination allows the opioid analgesic dosage to be lower, limiting side effects. The use of oxycodone 5 mg/ibuprofen 400 mg combination provided significantly better analgesia, in patients with moderate to severe pain, compared with other opioid/non-opioid combinations and were associated with fewer adverse events (14). Recent recommendations, compiled from literature, recommend a dosing of ibuprofen 400mg with APAP 500mg every 6 hours for moderate to severe postoperative dental pain (15).

CONCLUSION

Pain is one of the most common reasons patients seek dental treatment. Dentists must be able to diagnose the source of pain and have strategies for its management. These strategies should include the use of local anesthesia to break the pain cycle as well as the proper use of analgesics taken by the clock for pain relief. Postoperative acute pain may occur following endodontic treatment and can be controlled with analgesics. All clinicians are responsible for knowing their patients and prescribing appropriate medications to provide suitable pain relief.

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PAIN SEVERITY	ANALGESIC RECOMMENDATION
Mild	Ibuprofen 200-400mg q4-6 hrs: prn for pain
Mild to Moderate	Ibuprofen 400-600mg q6 hrs: fixed interval for 24 hours Then Ibuprofen 400mg q4-6hrs: prn for pain
Moderate to Severe	Ibuprofen 400-600mg with APAP 500mg q6hrs: fixed interval for 24 hours Then Ibuprofen 400mg with APAP 500mg q6hrs: prn for pain
Severe	Ibuprofen (400-600mg) with APAP (650mg) with hydrocodone (10mg) q 6 hrs: fixed interval for 24-48 hours. Then Ibuprofen (400-600mg) with APAP (500mg) q 6 hrs: prn for pain

Table adapted from Moore PA, Hersh EV. Combining ibuprofen and acetaminophen for acute pain management after third-molar extractions: Translating clinical research to dental practice. J Am Dent Assoc 2013; 144(8):898-908.

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